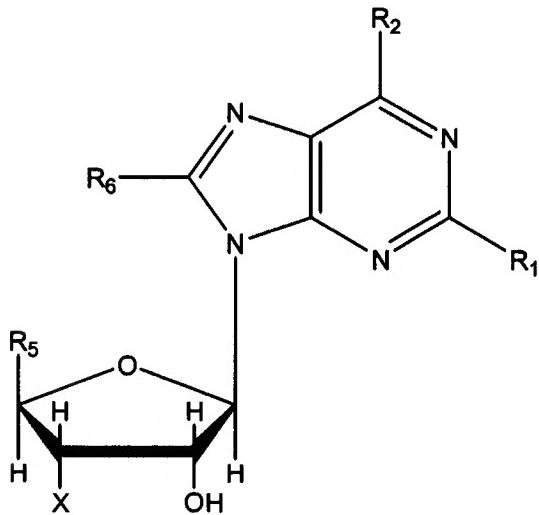


Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Original) A compound of the following general formula, or a pharmaceutically acceptable salt thereof, for use as a medicament:



wherein:

(I) when X = OH, R₂ = NH₂, R₅ = CH₂OH, R₆ = H, R₁ is C₅-C₆ alkoxy, OCH₂Cyclopropyl, OCH₂Cyclopentyl, O-(2,2,3,3-tetrafluoro-cycloButyl), phenoxy, substituted phenoxy, OCH₂CH₂OH, or OCH₂CHF₂, (5-indanyl)oxy, C₁, C₂, C₅, or C₆ alkylamino, (R) or (S)-sec-Butylamino, C₅ or C₆ cycloalkylamino, exo-norbornane amino, (N-methyl, N-isoamylamino),

phenylamino, phenylamino with either methoxy or fluoro substituents, a C₂ sulfone group, a C₇ alkyl group, a cyano group, a CONH₂ group, or 3,5-dimethylphenyl; or
when X = H, R₂ = NH₂, R₅ = CH₂OH, R₆ = H, R₁ is *n*-hexyloxy; or

(II) when X = OH, R₁ = H, R₅ = CH₂OH, R₆ = H, R₂ is NMe₂, N-(2-isopentenyl), piperazinyl, (N-Me, N-benzyl), (N-Me, N-CH₂Ph(3-Br)), (N-Me, N-CH₂Ph(3-CF₃)), or (N-Me, N-(2-methoxyethyl)), or OCH₂Cyclopentyl; or

(III) when X = OH, R₅ = CONHR₃, R₆ = H:

R₁ is H, R₃ is an isopropyl group, and R₂ is either NH₂ or a methylamino group (NHMe) or an isoamyl group (CH₂CH₂CHMe₂); or

R₁ is H, R₃ is H, and R₂ is NH₂; or

R₁ is OMe, R₃ is Ph, and R₂ is NH₂; or

R₁ is NHCH₂CH₂CH₂CH₂CH₂Me, R₃ is CH₂CH₂CH₂Me, and R₂ is NH₂; or

(IV) when X = OH, R₁ = H, R₂ = NH₂, R₅ = CH₂NHCOR₄, R₆ = H, R₄ is *n*-propyl or NHCH₂CH₃; or

(V) when X = OH, R₅ = CH₂OH, R₆ = H:

R₁ is NHCyclohexyl when R₂ is NMe₂; or

R₁ is OMe when R₂ is NH-Benzyl; or

(VI) when X = OH, R₂ = NH₂, R₅ = CH₂OH, R₆ = Me, R₁ is NHCyclohexyl, NHCyclopentyl, or NH-n-Hexyl.

2. (Original) A compound according to formula (I) of claim 1, or a pharmaceutically acceptable salt thereof, for use as a medicament, wherein when X is OH, R₂ is NH₂, R₅ is CH₂OH, and R₆ is H, R₁ is phenoxy substituted with 4-nitrile, 4-methyl, 3-phenyl, 3-bromo, 3-

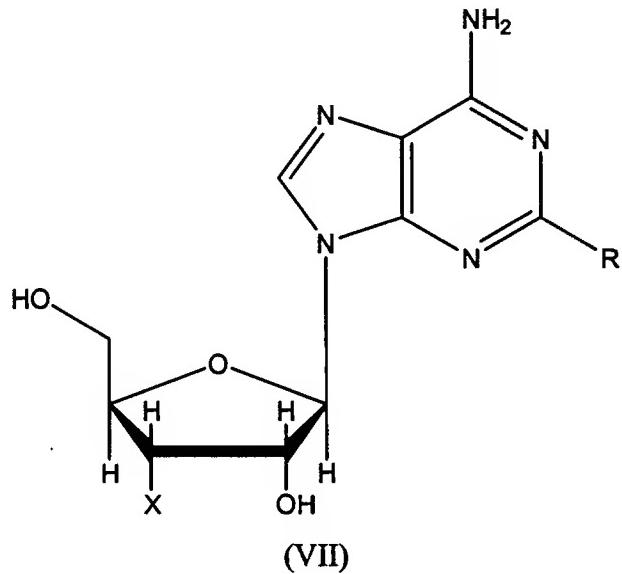
isopropyl, 2-methyl, 2,4-difluoro, 2,5-difluoro, 3,4-difluoro, 2,3,5-trifluoro, or (3-methyl,4-fluoro).

3. (Currently Amended) A compound according to claim 1 ~~or 2~~, with a structure as defined in any of Examples 1-6, or a pharmaceutically acceptable salt thereof, for use as a medicament.

4. (Original) A compound according to claim 3, with a structure corresponding to any of compound numbers 2, 3, 7-19, 22-25, 28, 31-33, or 35-60 as defined in Examples 1-6, or a pharmaceutically acceptable salt thereof, for use as a medicament.

5. (Original) A compound according to claim 3, with a structure corresponding to any of compound numbers 2, 3, 7-18, 22-25, 31-33, 35, 37, 40, 44, 45, 47, 48, or 51-60 as defined in Examples 1-6, or a pharmaceutically acceptable salt thereof, for use as a medicament.

6. (Currently Amended) Use of a compound as defined in any preceding claim, or a pharmaceutically acceptable salt of a compound of formula (VII), in the manufacture of a medicament for the prevention, treatment, or amelioration of a pathological condition that can be improved or prevented by agonism of adenosine A2A receptors:



wherein: R is C₁-4 alkoxy, and X is H or OH.

7-28. (Cancelled)

29. (Original) A compound with a structure corresponding to any of compound numbers 2, 3, 7-18, 22-25, 31-33, 35, 37, 40, 44, 45, 47, 48, or 51-60 as defined in Examples 1-6, or a pharmaceutically acceptable salt thereof.

30. (Currently Amended) A method of preventing, treating, or ameliorating a pathological condition that can be prevented or improved by agonism of adenosine A2A receptors, which comprises administering a compound as defined in claim 1 ~~any of claims 1 to 5, or a pharmaceutically acceptable salt of a compound of formula (VII) as defined in claim 6,~~ to a subject in need of such prevention, treatment, or amelioration.

31. (Original) A method of preventing, treating, or ameliorating a pathological condition that can be prevented or improved by agonism of adenosine A2A receptors, excluding pain, cancer, inflammation, auto-immune disease, ischemia-reperfusion injury, epilepsy, sepsis, septic

shock, neurodegeneration (including Alzheimer's Disease), muscle fatigue and muscle cramp, which comprises administering a compound of formula (VII) as defined in claim 6 to a subject in need of such prevention, treatment, or amelioration.

32. (Currently Amended) A method of preventing, treating, or ameliorating pain which comprises administering a compound as defined in claim 1 any of claims 1 to 5, or a pharmaceutically acceptable salt of a compound of formula (VII) as defined in claim 6, to a subject in need of such prevention, treatment, or amelioration.

33. (Currently Amended) A method of preventing, treating, or ameliorating ischaemic pain which comprises administering a compound as defined in claim 1 any of claims 1 to 5, or a compound of formula (VII) as defined in claim 6 or a pharmaceutically acceptable salt thereof, to a subject in need of such prevention, treatment, or amelioration.

34. (Original) A method according to claim 33 for the prevention, treatment, or amelioration of ischaemic pain associated with coronary artery disease, peripheral artery disease, left ventricular hypertrophy, essential hypertension, acute hypertensive emergency, cardiomyopathy, heart insufficiency, exercise tolerance, chronic heart failure, arrhythmia, cardiac dysrhythmia, syncope, arteriosclerosis, mild chronic heart failure, angina pectoris, Prinzmetal's (variant) angina, stable angina, exercise induced angina, cardiac bypass reocclusion, intermittent claudication (arteriosclerosis obliterens), arteritis, diastolic dysfunction, systolic dysfunction, atherosclerosis, post ischaemia/reperfusion injury, diabetes (Types I or II), thromboembolisms, haemorrhagic accidents, or neuropathic or inflammatory pain arising from hypoxia-induced nerve cell damage.

35. (Currently Amended) A method of prevention, treatment, or amelioration of inflammation, which comprises administering a compound as defined in claim 1 any of claims 1

~~to 5, or a pharmaceutically acceptable salt of a compound of formula (VII) as defined in claim 6,~~
to a subject in need of such prevention, treatment, or amelioration.

36. (Original) A method according to claim 35 for the prevention, treatment, or amelioration of inflammation caused by or associated with: cancer (such as leukemias, lymphomas, carcinomas, colon cancer, breast cancer, lung cancer, pancreatic cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic, lung, breast, and prostate metastases, etc.); auto-immune disease (such as organ transplant rejection, lupus erythematosus, graft v. host rejection, allograft rejections, multiple sclerosis, rheumatoid arthritis, type I diabetes mellitus including the destruction of pancreatic islets leading to diabetes and the inflammatory consequences of diabetes); autoimmune damage (including multiple sclerosis, Guillam Barre Syndrome, myasthenia gravis); obesity; cardiovascular conditions associated with poor tissue perfusion and inflammation (such as atheromas, atherosclerosis, stroke, ischaemia-reperfusion injury, claudication, congestive heart failure, vasculitis, haemorrhagic shock, vasospasm following subarachnoid haemorrhage, vasospasm following cerebrovascular accident, pleuritis, pericarditis, the cardiovascular complications of diabetes); ischaemia-reperfusion injury, ischaemia and associated inflammation, restenosis following angioplasty and inflammatory aneurysms; epilepsy, neurodegeneration (including Alzheimer's Disease), muscle fatigue or muscle cramp (particularly athletes' cramp), arthritis (such as rheumatoid arthritis, osteoarthritis, rheumatoid spondylitis, gouty arthritis), fibrosis (for example of the lung, skin and liver), sepsis, septic shock, encephalitis, infectious arthritis, Jarisch-Herxheimer reaction, shingles, toxic shock, cerebral malaria, Lyme's disease, endotoxic shock, gram negative shock, haemorrhagic shock, hepatitis (arising both from tissue damage or viral infection), deep vein thrombosis, gout; conditions associated with breathing difficulties (e.g. chronic obstructive pulmonary disease, impeded and obstructed airways, bronchoconstriction, pulmonary vasoconstriction, impeded respiration, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcosis, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, bronchial allergy and/or inflammation, asthma, hay fever, rhinitis, vernal conjunctivitis and adult respiratory

distress syndrome); conditions associated with inflammation of the skin (including psoriasis, eczema, ulcers, contact dermatitis); conditions associated with inflammation of the bowel (including Crohn's disease, ulcerative colitis and pyresis, irritable bowel syndrome, inflammatory bowel disease); HIV (particularly HIV infection), bacterial meningitis, TNF-enhanced HIV replication, TNF inhibition of AZT and DDI activity, osteoporosis and other bone resorption diseases, osteoarthritis, rheumatoid arthritis, infertility from endometriosis, fever and myalgia due to infection, cachexia secondary to cancer, cachexia secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome (AIDS), AIDS related complex (ARC), keloid formation, scar tissue formation, adverse effects from amphotericin B treatment, adverse effects from interleukin-2 treatment, adverse effects from OKT3 treatment, or adverse effects from GM-CSF treatment, and other conditions mediated by excessive anti-inflammatory cell (including neutrophil, eosinophil, macrophage and T- cell) activity.

37. (Currently Amended) A method of preventing, treating, or ameliorating macro or micro vascular complications of type 1 and 2 diabetes, retinopathy, nephropathy, autonomic neuropathy, or blood vessel damage caused by ischaemia or atherosclerosis which comprises administering a compound as defined in claim 1 any of claims 1 to 5, or a compound of formula (VII) as defined in claim 6 or a pharmaceutically acceptable salt thereof, to a subject in need of such prevention, treatment, or amelioration.

38. (Currently Amended) A method of slowing the progression of arthropathy, which comprises administering a compound as defined in claim 1 any of claims 1 to 5, or a compound of formula (VII) as defined in claim 6 or a pharmaceutically acceptable salt thereof, as a disease-modifying antirheumatic drug (DMARD) to a subject in need thereof.

39. (Original) A method according to claim 38, for slowing the progression of rheumatoid arthritis.

40. (Currently Amended) A method according to claim 30 any of claims 30 to 39, wherein the compound is administered at a dose that gives rise to a peak plasma concentration of the compound that is less than the EC50 value of the compound at adenosine receptors at pH 7.4.

41. (Currently Amended) A method according to claim 30 any of claims 30 to 40, wherein the compound is administered to the subject in an amount that results in a peak plasma concentration of the compound in the subject that is one ten thousandth to one half of the lowest EC50 value of the compound at adenosine receptors.

42. (Currently Amended) A method according to claim 30 any of claims 30 to 41, wherein the compound is administered to the subject in an amount that results in a plasma concentration of the compound in the subject being maintained for more than one hour at one ten thousandth to one half of the lowest EC50 value of the compound at adenosine receptors.

43. (Currently Amended) A method according to claim 30 any of claims 30 to 42, wherein the compound is administered to the subject in an amount that results in a peak plasma concentration of the compound in the subject that is one ten thousandth to one half of the lowest Kd value of the compound at adenosine receptors.

44. (Currently Amended) A method according to claim 30 any of claims 30 to 43, wherein the compound is administered to the subject in an amount that results in a plasma concentration of the compound in the subject being maintained for more than one hour at one ten thousandth to one half of the lowest Kd value of the compound at adenosine receptors.

45. (Currently Amended) A method according to claim 30 any of claims 30 to 44, wherein the compound is administered to the subject in an amount that is one ten thousandth to one half of the minimum amount of the compound that gives rise to bradycardia, hypotension or

tachycardia side effects in animals of the same species as the subject to which the compound is administered.

46. (Currently Amended) A method according to claim 30 any of claims 30 to 45, wherein the compound is administered at a dose that is one thousandth to one half of the minimum dose of the compound that gives rise to bradycardia, hypotension or tachycardia side effects in animals of the same species as the subject to which the dose is to be administered.

47. (Currently Amended) A method according to claim 46, wherein the dose is one hundredth to one half of the minimum dose that gives rise to the side effects.

48. (Currently Amended) A method according to claim 30 any of claims 30 to 47, wherein the compound is administered to the subject in an amount that results in a plasma concentration of the compound in the subject being maintained for more than one hour at one ten thousandth to one half of the minimum plasma concentration of the compound that gives rise to bradycardia, hypotension or tachycardia side effects in animals of the same species as the subject to which the compound is administered.

49. (Currently Amended) A method according to claim 30 any of claims 30 to 48, wherein the compound is administered at a dose that results in a plasma concentration of the compound that is maintained for more than one hour between one hundredth and one half of the minimum dose of the compound that gives rise to bradycardia, hypotension or tachycardia side effects in animals of the same species as the subject to which the compound is to be administered.

50. (Currently Amended) A method according to claim 30 any of claims 30 to 49, wherein the compound is administered at a dose of less than 0.4mg/kg.

51. (Currently Amended) A method according to claim 30 ~~any of claims 30 to 50~~, wherein the compound is administered at a dosage of 0.001 to 0.4mg/kg.

52. (Currently Amended) A method according to claim 30 ~~any of claims 30 to 51~~, wherein the compound is administered at a dose of at least 0.003mg/kg.

53. (Currently Amended) A method according to claim 30 ~~any of claims 30 to 52~~, wherein the compound is administered at a dose of 0.01 to 0.1mg/kg.

54. (Currently Amended) A method according to claim 30 ~~any of claims 30 to 53~~, wherein the compound is administered orally, parenterally, sublingually, transdermally, intrathecally, transmucosally, intravenously, intramuscularly, subcutaneously, topically, or by inhaling.

55. (Currently Amended) A method according to claim 30 ~~any of claims 30 to 54~~, wherein the compound is administered at a frequency of 2 or 3 times per day.

56. (Currently Amended) A method according to claim 30 ~~any of claims 30 to 55~~, wherein the subject is a human subject.

57. (Currently Amended) ~~A Use according to claim 20 or 21, or a~~ method according to claim 38 ~~or 39~~, wherein the compound is spongiosine or a pharmaceutically acceptable salt thereof.

58. (Currently Amended) A pharmaceutical composition in unit dose form comprising up to 500mg of a compound as defined in claim 1 ~~any of claims 1 to 5, excluding 2-phenylamino adenosine~~, and a physiologically acceptable carrier, excipient, or diluent.

59. (Currently Amended) A pharmaceutical composition in unit dose form comprising up to 500mg of a compound as defined in claim 1 ~~any of claims 1 to 5, or a compound of formula (VII) as defined in claim 6 or a pharmaceutically acceptable salt thereof,~~ together with an NSAID or a DMARD, and a physiologically acceptable carrier, excipient, or diluent.

60. (Original) A method of producing compound number 2 or 32 as defined in Example 1, which comprises reacting pentabenzoyl-2-nitro-adenosine with ROH, and deprotecting the reaction product to produce compound number 2 or 32, wherein R = CH₂CHF₂ or CH₂cyclopentyl.

61. (Original) A method of producing compound number 3 or 35 as defined in Example 1, which comprises reacting triacetoxy-6-chloro-2-nitro-adenosine with ROH, and deprotecting the reaction product to produce compound number 3 or 35, wherein R = CH₂Cyclopropyl or 2,2,3,3-tetrafluorocyclobutane.

62. (Original) A method of producing any of compound numbers 7-18 as defined in Example 1, which comprises reacting pentabenzoyl-2-nitro-adenosine with ArOH, and deprotecting the reaction product to produce any of compound numbers 7-18, wherein Ar = 4-cyanophenyl, 3-phenyl-phenyl, 2,5-difluorophenyl, 2,4-difluorophenyl, 3,4-difluorophenyl, 2,3,5-trifluorophenyl, 3-methyl,4-fluorophenyl, 2-methylphenyl, 3-bromophenyl, 4-methylphenyl, 5-indanyl, or 3-isopropylphenyl.

63. (Original) A method of producing any of compound numbers 22-25 or 31 as defined in Example 1, which comprises reacting 2-chloroadenosine with RR'NH to produce any of compound numbers 22-25 or 31, wherein RR'N = NH-(R)-sec-butyl, NH-(S)-sec-butyl, NH-n-Hexyl, NH-exo-norbornane, or N(Me)isoamyl.

64. (Original) A method of producing compound number 33 as defined in Example 1, which comprises reacting 2-chloro-adenosine with NaSEt to produce 2-ethylthio-adenosine, then producing compound number 33 from the 2-ethylthio-adenosine.

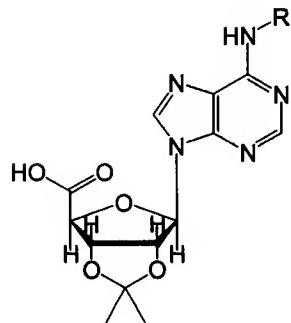
65. (Original) A method of producing compound number 37 as defined in Example 1, which comprises reacting 2-iodo-adenosine with ArB(OH)₂, wherein Ar = 3,5-dimethylphenyl.

66. (Original) A method of producing compound 40 as defined in Example 1, which comprises reacting 3'-deoxy-tetrabenzoyl-2-nitro-adenosine with n-hexanol, and deprotecting the reaction product to produce compound number 40.

67. (Original) A method of producing compound number 44, 45, or 47 as defined in Example 2, which comprises reacting 6-chloro-adenosine with RR'NH, wherein RR'N = N(Me)CH₂(3-bromophenyl), N(Me)CH₂(3-trifluoromethylphenyl), or N(Me)CH₂CH₂OMe.

68. (Original) A method of producing compound number 48 as defined in Example 2, which comprises reacting tri-acetoxy-6-chloro-adenosine with cyclopentylmethyl alcohol and deprotecting the reaction product to produce compound number 48.

69. (Original) A method of producing compound number 51 or 52 as defined in Example 3, which comprises reacting 2',3'-O-isopropylidene-6-alkylamino-adenosine-5'-carboxylic acid of the following formula:



wherein R = Me or isoamyl;

with isopropylamine, and deprotecting the acetonide group of the reaction product to produce compound number 51 or 52.

70. (Original) A method of producing compound number 53 as defined in Example 3, which comprises reacting 2',3'-O-isopropylidene-2-methoxy-adenosine-5'-carboxylic acid with aniline, and deprotecting the acetonide group of the reaction product to produce compound number 53.

71. (Original) A method of producing compound number 54 as defined in Example 3, which comprises reacting 2',3'-O-isopropylidene-2-chloro-adenosine-5'-carboxylic acid with n-hexylamine, reacting the reaction product with n-Butylamine, and deprotecting the acetonide group of the product of the reaction with n-Butylamine to produce compound number 54.

72. (Original) A method of producing compound number 55 as defined in Example 4, which comprises reacting 2',3'-O-isopropylidene-5'-amino-adenosine with butyric acid, and deprotecting the acetonide group of the reaction product to produce compound number 55.

73. (Original) A method of producing compound number 56 as defined in Example 4, which comprises reacting 2',3'-O-isopropylidene-5'-amino-adenosine with ethyl isocyanate, and deprotecting the acetonide group of the reaction product to produce compound number 56.

74. (Original) A method of producing compound number 57 as defined in Example 5, which comprises reacting tri-acetoxy-6-chloro-2-nitro-adenosine with dimethylamine, reacting the reaction product with cyclohexylamine, and deprotecting the product of the reaction with cyclohexylamine to produce compound 57.

75. (Original) A method of producing compound number 58 as defined in Example 5, which comprises reacting tri-acetoxy-6-chloro-2-nitro-adenosine with benzylamine, and reacting the reaction product with methoxide anion and deprotecting the protected groups to produce compound 58.

76. (Original) A method of producing compound any of compounds 59-61 as defined in Example 6, which comprises reacting 2-chloro-8-methyl-adenosine with RNH_2 , wherein R is Cyclohexyl, Cyclopentyl, or n-hexyl, to produce compound number 59, 60, or 61.